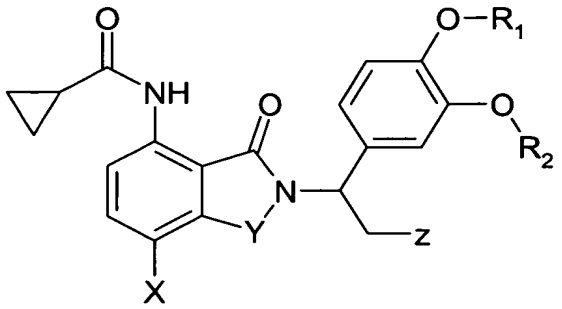
WHAT IS CLAIMED IS:

1. A compound of formula (**I**):



wherein:

Y is -C(O)-, -CH_2-, -CH_2C(O)- or -SO_2-;

X is H;

Z is (C_{0-4}-alkyl)-C(O)R^3, C_{1-4}-alkyl, (C_{0-4}-alkyl)-OH, (C_{1-4}-alkyl)-O-(C_{1-4}-alkyl), (C_{1-4}-alkyl)-SO_2(C_{1-4}-alkyl), (C_{0-4}-alkyl)-SO(C_{1-4}-alkyl), (C_{0-4}-alkyl)-NH_2, (C_{0-4}-alkyl)-N(C_{1-8}-alkyl)$_2$, (C_{0-4}-alkyl)-N(H)(OH), (C_{0-4}-alkyl)-dichloropyridine, or CH_2NSO_2-(C_{1-4}-alkyl);

R_1 and R_2 are independently C_{1-8}-alkyl, cycloalkyl, or (C_{1-4}-alkyl)-cycloalkyl;

R^3 is, NR^4 R^5, OH, or O-(C_{1-8}-alkyl);

R^4 is H;

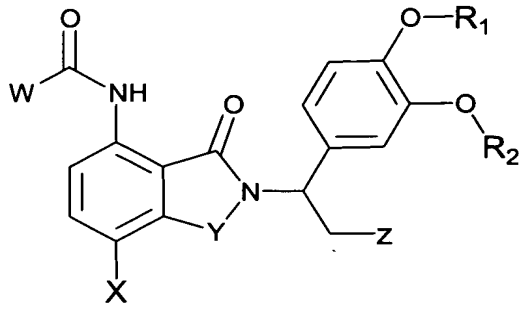
R^5 is -OH, or -O-C(O)R^6;

R^6 is C_{1-8}-alkyl, amino-(C_{1-8}-alkyl), (C_{1-8}-alkyl)-(C_{3-6}-cycloalkyl), C_{3-6}-cycloalkyl, phenyl, benzyl, or aryl;

or a pharmaceutically acceptable salt or solvate thereof.

2. The compound of claim 1, wherein Z is (C_{0-4}-alkyl)-C(O)R^3, C_{1-4}-alkyl, (C_{0-4}-alkyl)-OH, (C_{1-4}-alkyl)-O(C_{1-4}-alkyl), (C_{1-4}-alkyl)-SO_2(C_{1-4}-alkyl), (C_{0-4}-alkyl)-SO(C_{1-4}-alkyl), (C_{0-4}-alkyl)-NH_2, (C_{0-4}-alkyl)-N(C_{1-8}-alkyl)$_2$, (C_{0-4}-alkyl)-N(H)(OH), or CH_2NSO_2(C_{1-4}-alkyl).

3. A compound of formula **(II)** :



wherein:

Y is -C(O)-, -CH_2-, -CH_2C(O)-, or -SO_2-;

X is halogen, CN, NR_7R_8, NO_2, CH_3, or CF_3;

Z is (C_{0-4}-alkyl)-SO_2(C_{1-4}-alkyl), (C_{0-4}-alkyl)-CN, (C_{0-4}-alkyl)-C(O)R^3, C_{1-4}-alkyl, (C_{0-4}-alkyl)-OH, (C_{0-4}-alkyl)-O-(C_{1-4}-alkyl), (C_{0-4}-alkyl)-SO(C_{1-4}-alkyl), (C_{0-4}-alkyl)-NH_2, (C_{0-4}-alkyl)-N(C_{1-8}-alkyl)$_2$, (C_{0-4}-alkyl)-N(H)(OH), (C_{0-4}-alkyl)-dichloropyridine, or (C_{0-4}-alkyl)-NSO_2(C1-4-alkyl);

W is C_{3-6}-cycloalkyl, (C_{1-8}-alkyl)-(C_{3-6}-cycloalkyl), (C_{0-8}-alkyl)-(C_{3-6}cycloalkyl)-NR_7R_8, (C_{0-8}-alkyl)-NR_7R_8, (C_{0-4}alkyl)-CHR_9-(C_{0-4}alkyl)-NR_7R_8,

R_1 and R_2 are independently C_{1-8}-alkyl, cycloalkyl, or (C_{1-4}-alkyl)-cycloalkyl;

R^3 is C_{1-8}-alkyl, NR^4 R^5, OH, or O-(C_{1-8}-alkyl);

R^4 and R^5 are independently H, C_{1-8}-alkyl, (C_{0-8}-alkyl)-(C_{3-6}-cycloalkyl), OH, or OC(O)R^6;

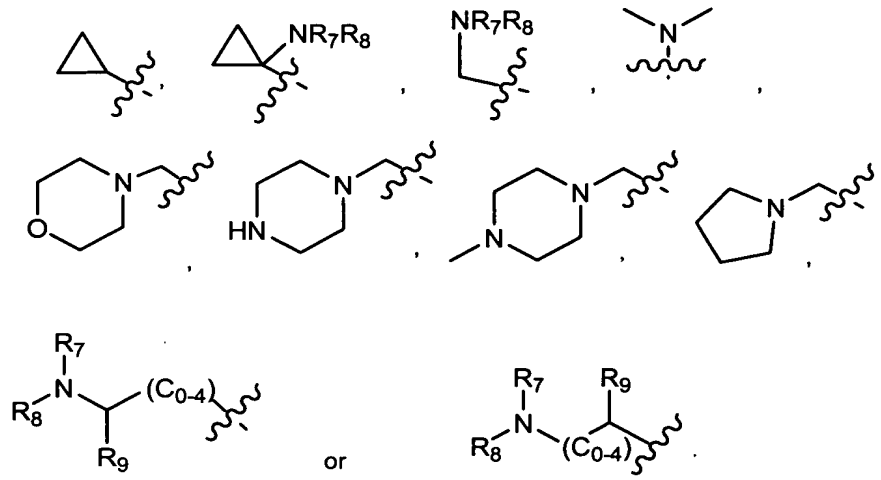
R^6 is C_{1-8}-alkyl, (C_{0-8}-alkyl)-(C_{3-6}-cycloalkyl), amino-(C_{1-8}-alkyl), phenyl, benzyl, or aryl;

R_7 and R_8 are each independently H, C_{1-8}-alkyl, (C_{0-8}-alkyl)-(C_{3-6}-cycloalkyl), phenyl, benzyl, aryl, or can be taken together with the atom connecting them to form a 3 to 7 membered heterocycloalkyl or heteroaryl ring;

R_9 is C_{1-4} alkyl, (C_{0-4}-alkyl)-aryl, (C_{0-4}-alkyl)-(C_{3-6}-cycloalkyl), (C_{0-4}alkyl)-heterocycle;R_9 is C_{1-4} alkyl, (C_{0-4}alkyl)aryl, (C_{0-4}alkyl)-(C_{3-6}cycloalkyl), (C_{0-4}alkyl)-heterocylcle;

or a pharmaceutically acceptable salt or solvate thereof.

4. The compound of claim 3, wherein W is:



or

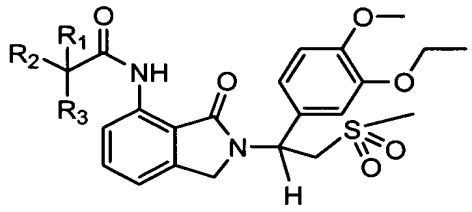
5. The compound of claim 1 or 3 wherein R_1 is CH_3.

6. The compound of claim 1 or 3 wherein R_2 is CH_2CH_3, CH_3, CH_2-cyclopropyl, or cyclopentyl.

7. The compound of claim 1 or 3 wherein Y is –C(O)- or -CH_2-.

8. The compound of claim 3 wherein X is fluoro, chloro or bromo.

9. A compound of formula (**III**):



wherein:

R_1, R_2 and R_3 are independently H or C_{1-8}-alkyl, with the proviso that at least one of R_1, R_2 and R_3 is not H;

or a pharmaceutically acceptable salt or solvate thereof.

10. The compound of claim 9, wherein R_1 is H and R_2 and R_3 are both methyl.

11. An enantiomerically pure S isomer of a compound of claim 1, 3 or 9, substantially free of its R isomer, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

12. An enantiomerically pure R isomer of a compound of claim 1, 3 or 9, substantially free of its S isomer, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

13. A compound, wherein the compound is:
(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-hydroxy-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(3R)-(tert-Butoxy)-N-{3-[7-(cyclopropylcarbonylamino)-1-oxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl}carbonylamino (tert-butoxy)formate;
(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-hydroxyamino-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-methanesulfonylamino-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(1R)-Cyclopropanecarboxylic acid {2-[3-amino-1-(3-ethoxy-4-methoxy-phenyl)-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-ureido-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(1R)-Cyclopropanecarboxylic acid {2-[3-dimethylamino-1-(3-ethoxy-4-methoxy-phenyl)-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide hydrochloride;
(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-methanesulfonyl-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(1R)- Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-hydroxycarbamoyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(1R)-Cyclopropanecarboxylic acid {2-[2-acetoxycarbamoyl-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(3R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-methanesulfinyl-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;
(3R)-3-[4-Chloro-7-(cyclopropanecarbonyl-amino)-1-oxo-1,3-dihydro-isoindol-2-yl]-3-(3-ethoxy-4-methoxy-phenyl)-propionic acid;

(3R)-3-[4-Chloro-7-(cyclopropanecarbonyl-amino)-1-oxo-1,3-dihydro-isoindol-2-yl]-3-(3-ethoxy-4-methoxy-phenyl)-propionic acid methyl ester;

(1R)-Cyclopropanecarboxylic acid {2-[2-carbamoyl-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-7-chloro-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

(1R)-Cyclopropanecarboxylic acid {7-chloro-2-[2-dimethylcarbamoyl-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

(1R)-Cyclopropanecarboxylic acid {7-chloro-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-hydroxycarbamoyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

(1R)-Cyclopropanecarboxylic acid {2-[2-acetoxycarbamoyl-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-7-chloro-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

(1S)-Cyclopropanecarboxylic acid {7-chloro-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

(1S)-Cyclopropanecarboxylic acid {7-bromo-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

Cyclopropanecarboxylic acid {2-[2-(3,5-dichloro-pyridin-4-yl)-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-hydroxy-3-methyl-butyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1R)-Cyclopropanecarboxylic acid {2-[2-cyclopropanecarbonyloxycarbamoyl-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-isobutyryloxycarbamoyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1R)-Cyclopropanecarboxylic acid {2-[2-(2,2-dimethyl-propionyloxycarbamoyl)-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1R)-Cyclopropanecarboxylic acid {2-[2-(3,3-dimethyl-butyryloxycarbamoyl)-1-(3-ethoxy-4-methoxy-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1S)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-7-fluoro-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide

(1S)-3-{7-Chloro-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-1,1-dimethyl-urea

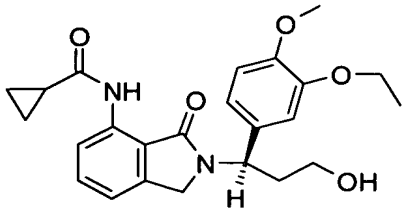
(1S)-N-{7-Chloro-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-

dihydro-1H-isoindol-4-yl}-2-(4-methyl-piperazin-1-yl)-acetamide

(1S)-N-{7-Chloro-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-2-morpholin-4-yl-acetamide; hydrochloride

(1S)-N-{7-Chloro-2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-2-dimethylamino-acetamide; hydrochloride

14. A compound of the formula: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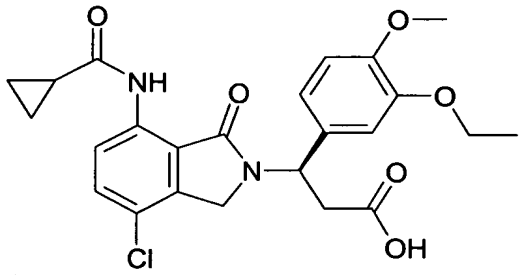
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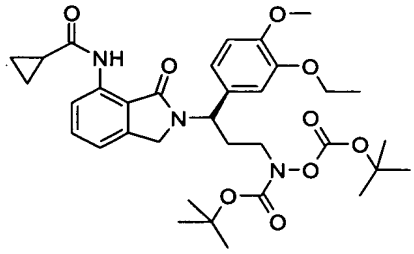
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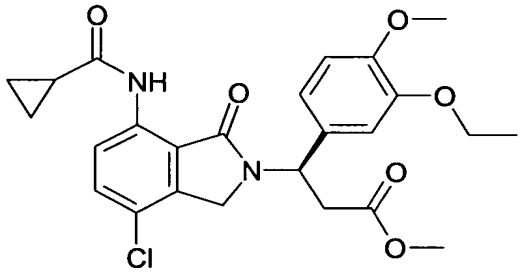
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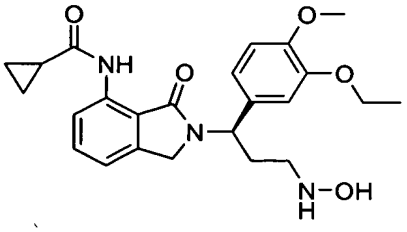
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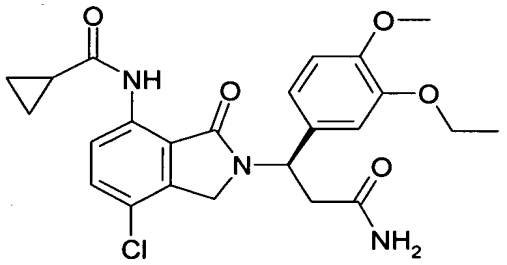
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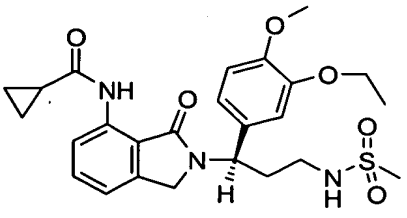
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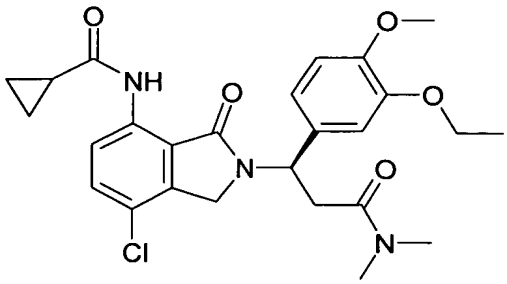
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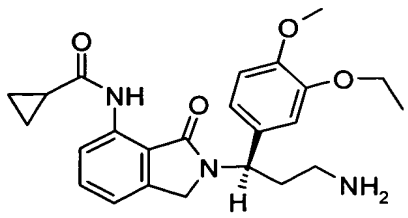
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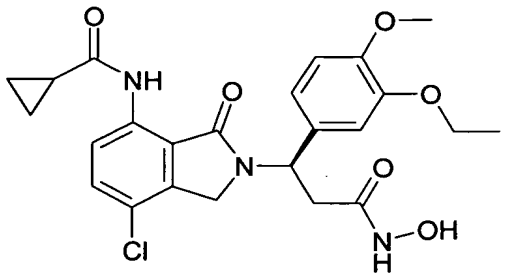
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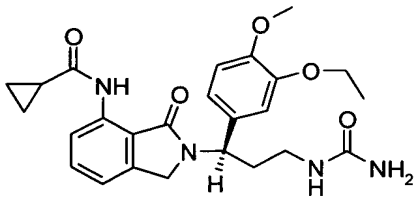
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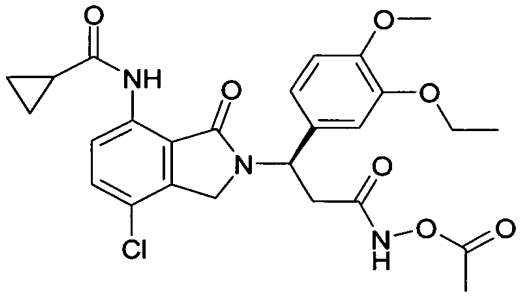
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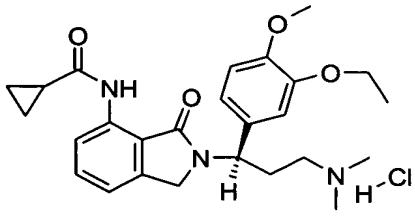
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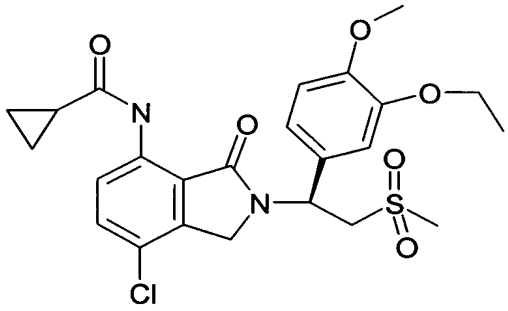
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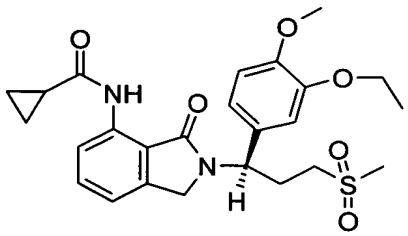
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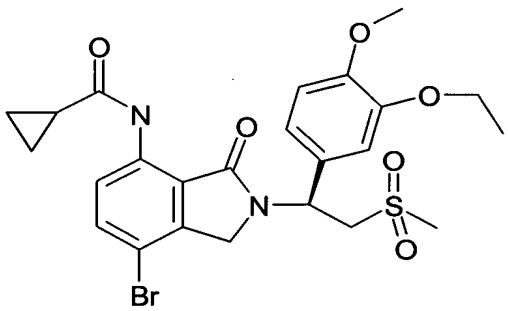
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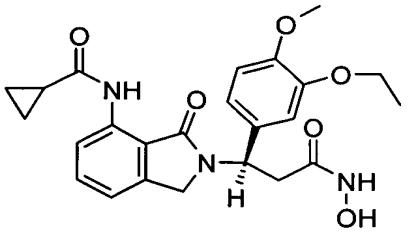
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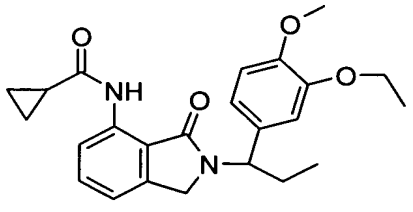
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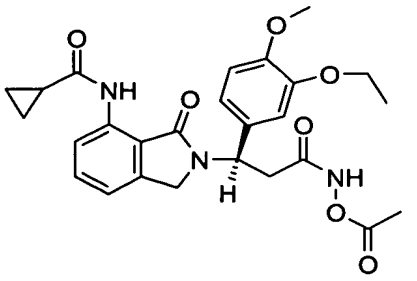
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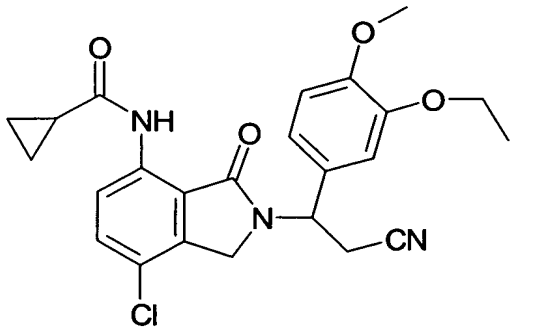
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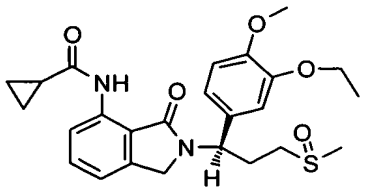
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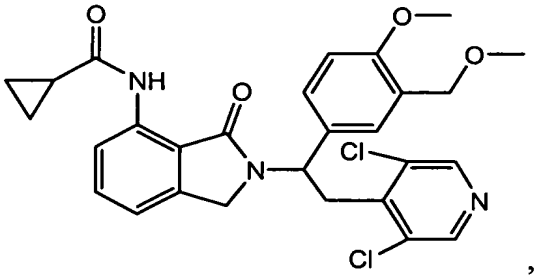
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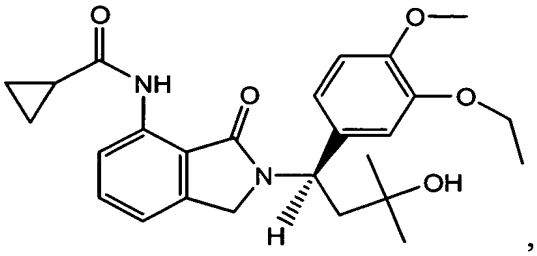
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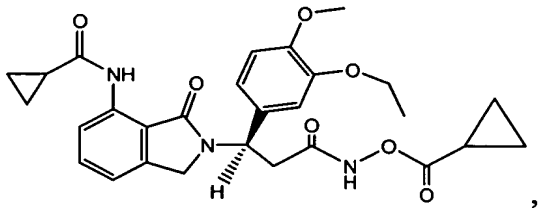
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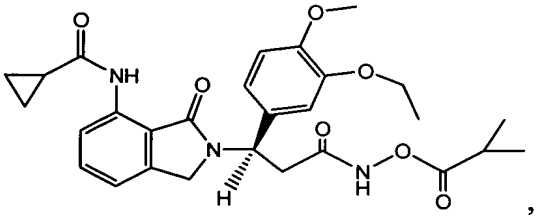
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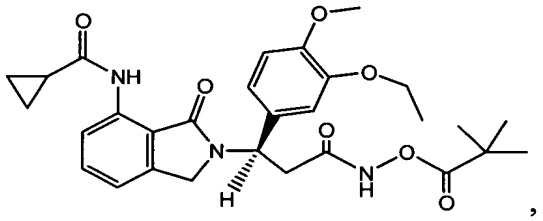
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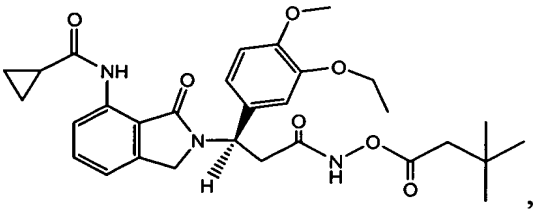
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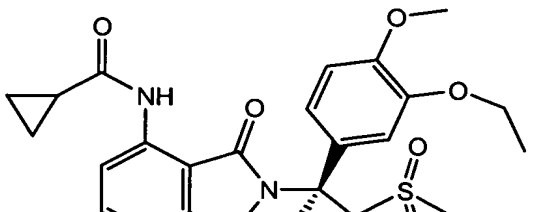
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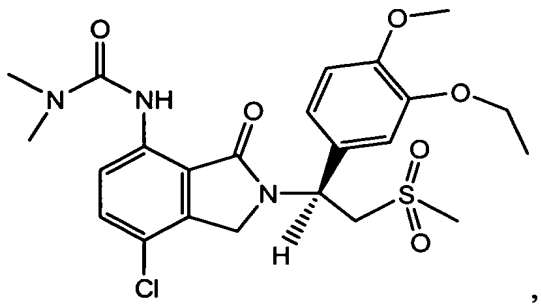
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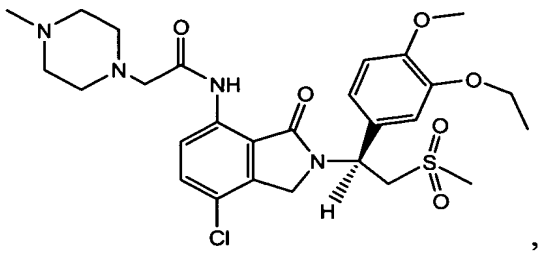
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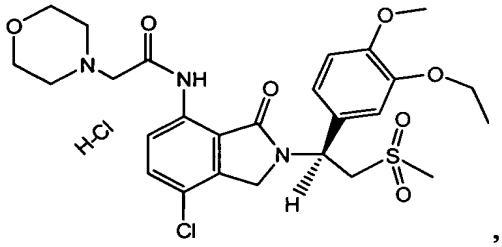
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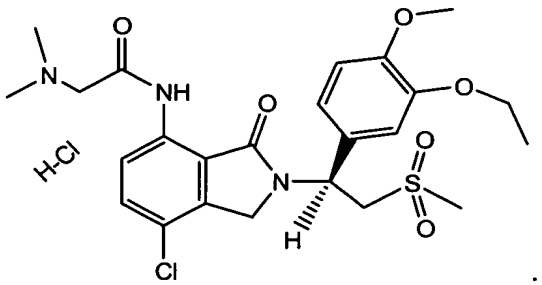
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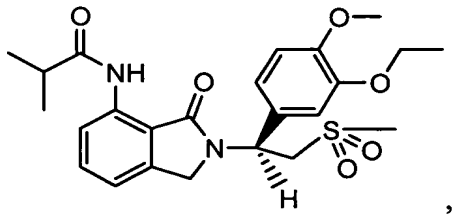
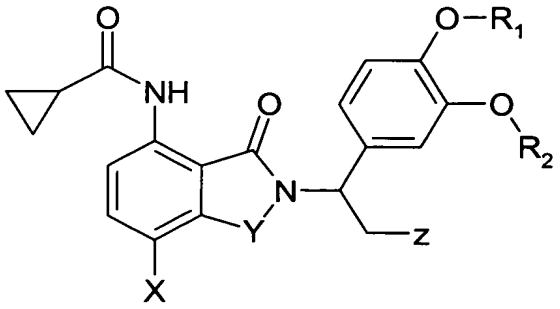
or a pharmaceutically acceptable salt or solvate thereof.

15. A compound of the formula:


,

or a pharmaceutically acceptable salt or solvate thereof.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient, or diluent and a compound of formula (**I**):



wherein:

Y is -C(O)-, -CH_2-, -CH_2C(O)- or -SO_2-;

X is H;

Z is (C_{0-4}-alkyl)-C(O)R^3, C_{1-4}-alkyl, (C_{0-4}-alkyl)-OH, (C_{1-4}-alkyl)-O-(C_{1-4}-alkyl), (C_{1-}

$_4$-alkyl)-SO_2(C_{1-4}-alkyl), (C_{0-4}-alkyl)-SO(C_{1-4}-alkyl), (C_{0-4}-alkyl)-NH_2, (C_{0-4}-alkyl)-N(C_{1-8}-alkyl)$_2$, (C_{0-4}-alkyl)-N(H)(OH), (C_{0-4}-alkyl)-dichloropyridine, or CH_2NSO_2-(C_{1-4}-alkyl);

R_1 and R_2 are independently C_{1-8}-alkyl, cycloalkyl, or (C_{1-4}-alkyl)-cycloalkyl;

R^3 is, NR^4 R^5, OH, or O-(C_{1-8}-alkyl);

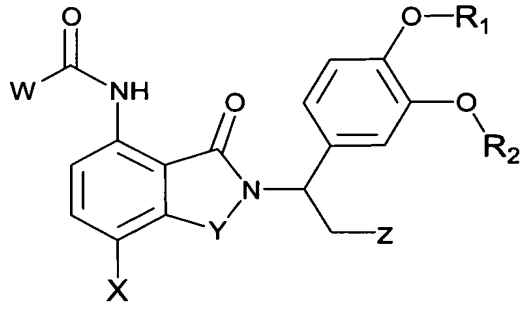
R^4 is H;

R^5 is -OH, or -O-C(O)R^6;

R^6 is C_{1-8}-alkyl, amino-(C_{1-8}-alkyl), (C_{1-8}-alkyl)-(C_{3-6}-cycloalkyl), C_{3-6}-cycloalkyl, phenyl, benzyl, or aryl;

or a pharmaceutically acceptable salt or solvate thereof.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient, or diluent and a compound of formula **(II)** :



wherein:

Y is -C(O)-, -CH_2-, -CH_2C(O)-, or -SO_2-;

X is halogen, CN, NR_7R_8, NO_2, CH_3, or CF_3;

Z is (C_{0-4}-alkyl)-SO_2(C_{1-4}-alkyl), (C_{0-4}-alkyl)-CN, (C_{0-4}-alkyl)-C(O)R^3, C_{1-4}-alkyl, (C_{0-4}-alkyl)-OH, (C_{0-4}-alkyl)-O-(C_{1-4}-alkyl), (C_{0-4}-alkyl)-SO(C_{1-4}-alkyl), (C_{0-4}-alkyl)-NH_2, (C_{0-4}-alkyl)-N(C_{1-8}-alkyl)$_2$, (C_{0-4}-alkyl)-N(H)(OH), (C_{0-4}-alkyl)-dichloropyridine, or (C_{0-4}-alkyl)-NSO_2(C1-4-alkyl);

W is C_{3-6}-cycloalkyl, (C_{1-8}-alkyl)-(C_{3-6}-cycloalkyl), (C_{0-8}-alkyl)-(C_{3-6}cycloalkyl)-NR_7R_8, (C_{0-8}-alkyl)-NR_7R_8, (C_{0-4}alkyl)-CHR_9-(C_{0-4}alkyl)-NR_7R_8,

R_1 and R_2 are independently C_{1-8}-alkyl, cycloalkyl, or (C_{1-4}-alkyl)-cycloalkyl;

R^3 is C_{1-8}-alkyl, NR^4 R^5, OH, or O-(C_{1-8}-alkyl);

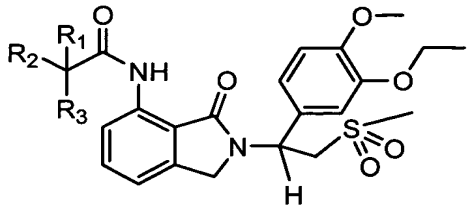
R^4 and R^5 are independently H, C_{1-8}-alkyl, (C_{0-8}-alkyl)-(C_{3-6}-cycloalkyl), OH, or OC(O)R^6;

R^6 is C_{1-8}-alkyl, (C_{0-8}-alkyl)-(C_{3-6}-cycloalkyl), amino-(C_{1-8}-alkyl), phenyl, benzyl, or aryl;

R_7 and R_8 are each independently H, C_{1-8}-alkyl, (C_{0-8}-alkyl)-(C_{3-6}-cycloalkyl), phenyl, benzyl, aryl, or can be taken together with the atom connecting them to form a 3 to 7 membered heterocycloalkyl or heteroaryl ring;

R_9 is C_{1-4} alkyl, (C_{0-4}-alkyl)-aryl, (C_{0-4}-alkyl)-(C_{3-6}-cycloalkyl), (C_{0-4}alkyl)-heterocycle;or a pharmaceutically acceptable salt or solvate thereof.

18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient, or diluent and a compound of formula **(III)**:



wherein:

R_1, R_2 and R_3 are independently H or C_{1-8}-alkyl, with the proviso that at least one of R_1, R_2 and R_3 is not H;

or a pharmaceutically acceptable salt or solvate thereof.

19. The pharmaceutical composition of claim 14, 15, or 16, further comprising an additional therapeutic agent.

20. The pharmaceutical composition of claim 19, wherein the additional therapeutic agent is an anti-cancer agent or an anti-inflammatory agent.

21. The pharmaceutical composition of claim 20, wherein the anti-cancer agent is paclitaxel, cisplatin, tamoxifen, docetaxel, pirubicin, doxorubicin, irinotecan, leuprolide, bicalutamide, a goserlin implant, gemcitabine, sargramostim or a steroid.

22. A method of inhibiting PDE4 in a mammal comprising administering to said mammal an effective amount of a compound of claim 1, 3, or 9.

23. A method of modulating the production of TNF-α in a mammal comprising administering to said mammal an effective amount of a compound of claim 1, 3, or 9.

24. A method of inhibiting MMP in a mammal comprising administering to said mammal an effective amount of a compound of claim 1, 3, or 9.

25. A method of treating, preventing or managing undesired angiogenesis in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

26. A method of treating, preventing or managing cancer in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

27. The method of claim 26, wherein the cancer is a solid tumor or a blood-born tumor.

28. The method of claim 27, wherein the cancer is of the skin; lymph node; breast; cervix; uterus; gastrointestinal tract; lung; ovary; prostate; colon; rectal; mouth; brain; head and neck; throat; testes; kidney; pancreas; bone; spleen; liver; bladder; larynx; or nasal passages.

29. A method of treating, preventing or managing a disease in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9, wherein the disease is an inflammatory disease, autoimmune disease, arthritis, rheumatoid arthritis, inflammatory bowel disease, Parkinson's disease, Crohn's disease, aphthous ulcers, cachexia, graft versus host disease, asthma, adult respiratory distress syndrome, inflammation of the lungs, depression, chronic obstructive pulmonary disorder, inflammatory bowel disease, atopic dermatitis, psoriasis or acquired immune deficiency syndrome.

30. A method of treating, preventing or managing asthma in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

31. The method of claim 30, wherein compound is administered via an inhaler.

32. A method of treating, preventing or managing multiple sclerosis in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

33. A method of treating, preventing or managing heart disease in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

34. A method of treating, preventing or managing chronic obstructive pulmonary disorder in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

35. A method of treating, preventing or managing inflammatory bowel disease in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

36. A method of treating, preventing or managing atopic dermatitis in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

37. A method of treating, preventing or managing Crohn's disease in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

38. A method of treating, preventing or managing rheumatoid arthritis in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

39. A method of treating, preventing or managing complex regional pain syndrome in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

40. A method of treating, preventing or managing a myeloproliverative disease in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

41. A method of treating, preventing or managing Myelodysplastic Syndrome in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

42. A method of treating, preventing or managing a central nervous disorder in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

43. A method of treating, preventing or managing macular degeneration in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

44. A method of treating, preventing or managing an asbestos-related disease or disorder in a patient which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1, 3, or 9.

45. The method of any one of claims 22-44, wherein the patient, the mammal or mammalian cell is human.